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Three-dimensional analysis of the spine in autopsy cases with renal osteodystrophy

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Three-dimensional analysis of the spine in autopsy cases with renal osteodystrophy. The spinal column was removed from nine autopsy cases with chronic maintenance dialysis and sectioned in the sagittal plane to a thickness of 1 millimeter using a surface-stained block grinding technique. A combination of two- and three-dimensional analysis included an evaluation of the spine deformity index (SDI), the bone volume (BV/TV), the trabecular interconnection (TBPf), the trabecular thickness (Tb.Th), the trabecular number (Tb.N) as well as a qualitative investigation of the structure of cancellous bone. The control group consisted of 26 autopsy cases with intact skeletons. An iliac crest biopsy made a direct comparison of the diagnostic biopsy location and the spinal column possible. The SDI showed vertebral fractures in renal osteodystrophy (ROD) of types I and II, in spite of a trabecular bone volume within normal limits. The trabecular bone volume showed mean values and a distribution throughout the spinal column familiar in the skeletally-intact control group. Those cases with a longer history of hemodialysis showed higher BV/TV values regardless of age and sex. A trabecular volume within normal limits did not mean physiological trabecular interconnection. Perforations were commonly observed with ROD. Classical, hidden and tunnelling perforations were distinguished. Microcallus formations were frequently seen in the periphery of vertebrae at rod nodes, rods and plate intersections. Three-dimensional analysis in ROD shows a greater alteration in architecture than can be assumed from the two-dimensional histological sections.

Patients with chronic renal insufficiency show changes in their skeletal system. The etiology of the symptoms has various causes, reflecting a secondary hyperparathyroidism, a vitamin D metabolic disorder, a parathyroid hormone resistance of the bone cells and iatrogenic influences (aluminum, excessive therapy). The polymorphism of these skeletal changes allows a differentiation of the morphological characteristics into three types of renal osteodystrophy (Table 1).

The prognosis for those patients with chronic renal disease depends on organic complications and the primary disease. However, since the 1960's and with the introduction of chronic hemodialysis, improved medical care and the possibility of kidney transplants, life expectancy has increased remarkably and thus the complications ascribed to the skeletal system gain importance. The quality of life for the patients can be considerably impaired by symptoms of renal osteodystrophy, by bone pain, fractures and joint complaints.

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It is the aim of this study to comprehensively record the structural changes of the spinal column from the axis to the fifth lumbar vertebra. This analysis deals with the following topics: (1.) Almost all morphological examinations have so far been carried out on the iliac crest bone biopsies. It was postulated that the changes in the spinal column, a decisive organ for human mobility, are the same. However, due to considerable problems in preparation procedures, hardly any morphological examinations of the spinal column exist. (2.) The structure of the spongiosa in ROD is exclusively known from slide material. Since only a limited evaluation of microarchitecture is possible from such sections, the three-dimensional spongiosa structure in renal osteodystrophy is unknown. Therefore, the combined two- and three-dimensional analysis of surface-stained block material is done.

Methods

Material

Spinal columns and iliac crest bone biopsies from nine autopsy cases (4 females, 5 males, median age 63.6 years) with long-term hemodialysis were removed for histological preparation. Hemodialysis lasted from 4 to 15 years. As a control group, the spinal columns of 26 normal autopsy cases (thirteen females, thirteen males) were used. For the comparison of the quantitative results the age-matched control group consists of 18 skeletal intact autopsy cases (> 40 years in age, 9 females, 9 males, median age 63.9 years).

Methods

The iliac crest biopsies were removed as described by Bordier et al [1] 2 cm below and behind the spina iliaca anterior superior. Then they were undecalcified embedded in plastic (methylmethacrylate) and cut into 5 μm thick slides. Histological evaluation was made with standard stainings (von Kossa, Goldner, Giemsa, Toluidin-blue, Berlin-blue reaction, Aluminon stain).

The preparation technique, as described below, was carried out on all of the spinal columns. After removal of the front column of the spine, a 4 mm thick sagittal segment was prepared with a diamond-coated saw and documented on x-rays (Fig. 1). Subsequently, the bone marrow was carefully rinsed with water.

Dehydration, fat removal and embedding of the material was carried out according to the method described by Hahn, Vogel and Delling [2]. The undecalcified material, embedded in plastic, was ground to a thickness of 1 mm, polished, and attached to slides. The surface was stained using a modification of the von

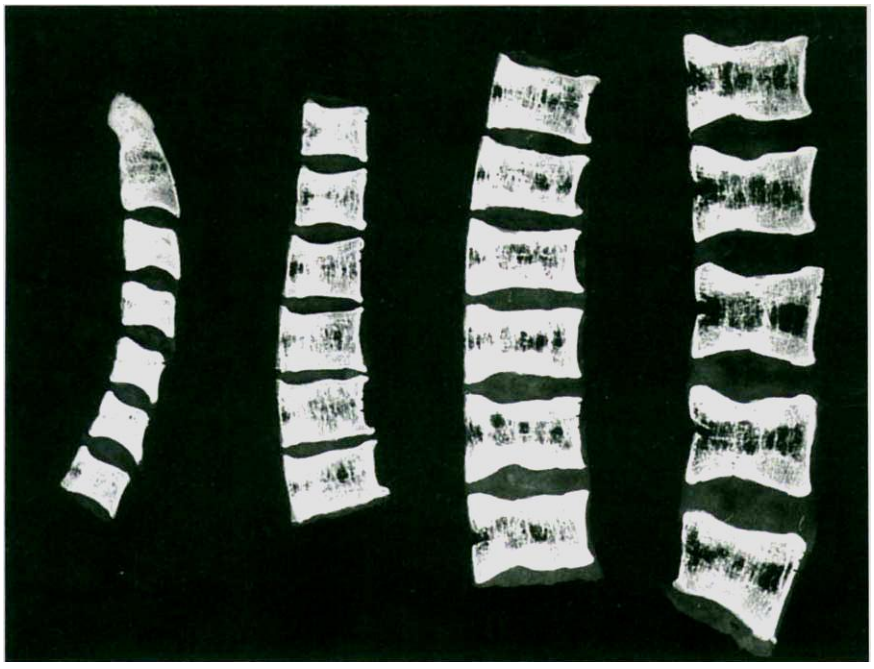


Fig. 1. *Contact X-ray of a 4 mm thick sagittal spinal segment for the purpose of documentation and determination of SDI.* Rubber-jersey-spine, ROD Type IIIc (scale 1:2.4).

Table 1. Morphological classification of renal osteodystrophy (Delling)

Type I	Fibroosteoclasia
Type II	Surface osteoidosis, volume and surface osteoidosis
Type III	Fibroosteoclasia and osteoidosis
Spongiosa reorganization	
a	lowered
b	normal or slightly increased
c	extremely increased, extensive fiber bone formation
Bone mass	
−	Osteopenia
+	Osteosclerosis

Kossa method [2]. The high contrast achieved by this silver-staining enables the subsequent evaluation by an automatic computer-assisted image analyzing system (IBAS 2000, Kontron, Germany). Because of the thickness of the specimens they could be analyzed in two- and three-dimensions simultaneously. Due to this technique it was possible to demonstrate the three-dimensional structure which was illuminated in dark field microscopy, as opposed to the transmission ligth microscopy, which only lets one see the two-dimensional structure.

Quantitative and qualitative evaluation of the spongiosa structure was carried out for each vertebra separately for five fields of measurement.

The following parameters were evaluated:

Spine Deformity Index (SDI). The index originally introduced by Minne et al [3] in 1988 for lateral x-rays of the spinal column quantifies the extent of the spinal deformity. It is based on the difference between expected and actual measured height of individual vertebra. As the fourth thoracic vertebra is, according to extensive studies, hardly deformed, it serves as an "internal" reference measurement. Due to the independence from the absolute hight of vertebrae the index is interindividually variable (Fig. 1).

Trabecular bone volume, bone volume per tissue volume (BV/TV; %). By means of a video camera the microscopic image of the specimen is transferred to an automatic image analyzing system (IBAS 2000, Kontron, Germany). The image analyzing system automatically measured the silver stained surface of trabeculae in each field of measurement, in relation to the whole measurement field of the vertebra block material examined. This procedure is equivalent to the commonly used two-dimensional analysis of cut sections.

Degree of trabecular interconnection, trabecular bone pattern factor (TBPf; per millimeter). The extent of interconnection of the trabeculae of cancellous bone was determined automatically by a procedure first developed by Hahn, Vogel and Delling [4]. Biomechanical stability of cancellous bone is determined not only by bone volume (BV/TV) but also by orientation and degree of interconnection of trabeculae, which is summarized as trabecular microarchitecture. TBPf quantifies the microarchitecture of cancellous bone by evaluating trabecular nodes. A higher TBPf-value implies a poor state of interconnection and vice versa.

Trabecular thickness (Tb.Th; μm). The semiautomatic measurement of Tb.Th (MOP, Videoplan, Kontron) was based on the orthogonal intercept length as the mean perpendicular distance from one trace of the trabecular surface to the other. The crossing points of the test lines, which were distributed at random, with the trabecular surface, served as fix-points from which the intercepts were measured orthogonically. One hundred and fifty to 200 intercepts per specimen were measured. Simultaneously, horizontal plates, vertical plates, horizontal rods and vertical rods were differentiated.

Trabecular number (Tb.N; mm^{-1}). Semiautomatic computer-aided measurement was done on Videoplan. The total number of all the sectioned structural elements (n) is divided by the total length of all the test lines (l) in millimeters:

$$Tb.N = n/l\,[mm^{-1}].$$

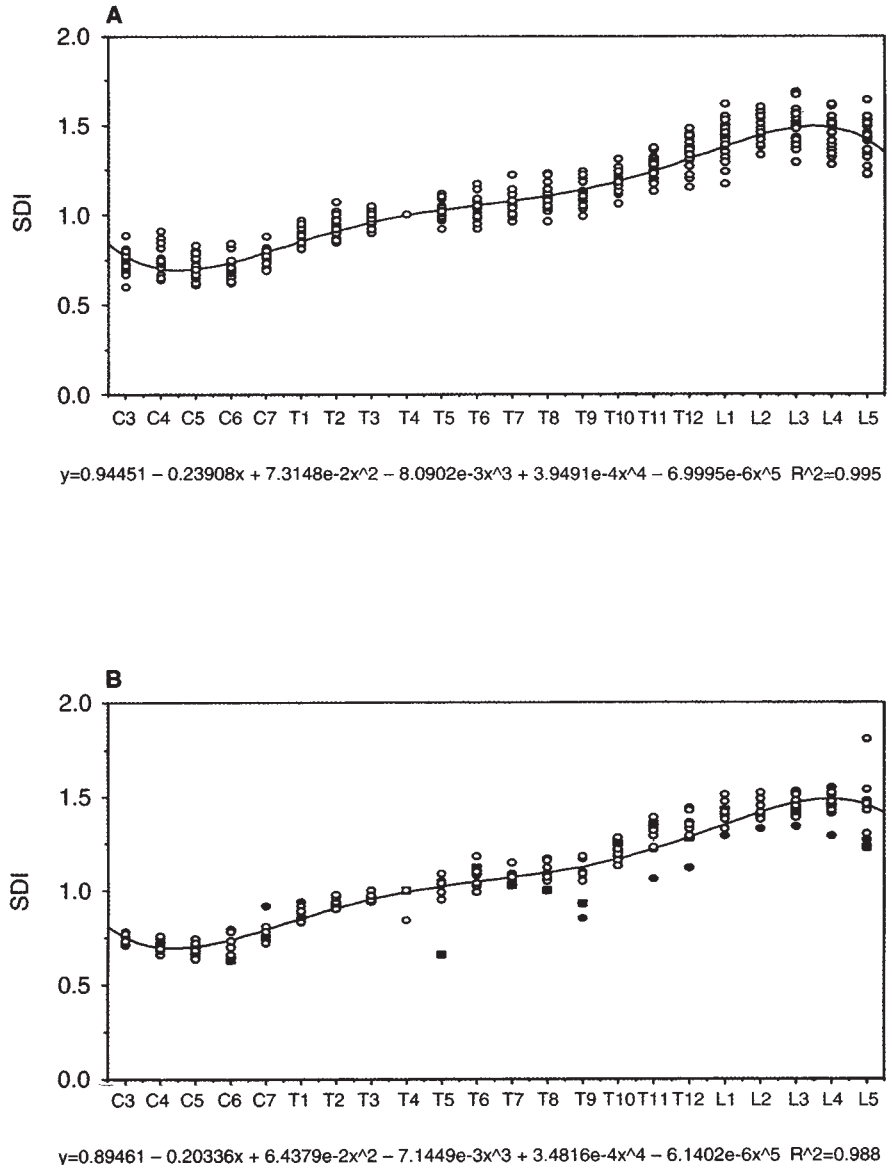


Fig. 2. A. *Spine deformity index (SDI) of 26 skeletally intact autopsy cases.* The lack of deformity of all the vertebra confirms the correct assignment, by medical history and histology, of these to the normal group. The median reference values correspond to those given by Minne et al in 1988 [3] and are illustrated on the diagram. **B.** Spine deformity index (SDI) of the 9 cases of renal osteodystrophy. Individual fractured vertebrae without significantly greater distribution. There are more often low SDI values in ROD types I and II, in comparison to type III. The course of the courve is comparable to that of the normal group.

Microcallus formations (qualitative). The evaluation covered both the two- and the three-dimensional view of the block grindings. The study was performed using a stereological microscope, because the three-dimensional study of bone structure was essential for correct interpretation of the silver stained structures on the surface.

The microcallus formations were the results of microfractures or local stress peaks in the spongy bone. The presence of microcallus was considered to be an indicator of static insufficiency. This static insufficiency must be regarded as a relative static insufficiency since it did not lead to a deformation of the outer shape of the vertebra. The relevance of microcallus formations is at present unknown. This could be a sign of repair procedures in relative static insufficiency of cancellous bone.

Perforations and free ends (qualitative). The illustration of trabeculae with free ends is only possible in three-dimensional analysis, but not on a stained surface. The evaluation was carried out using a stereological microscope. Due to perforations in the trabeculae their continuity is not given. As a result the trabeculae are disconnected from the trabecular lattice and unable to provide stability.

Results

Quantitative results

Types of renal osteodystrophy (ROD) according to Delling [5–7]. In all cases of chronic maintenance dialysis there was a varying degree of renal osteodystrophy which could be demonstrated. In nine cases there was a ROD Ia (once) and a ROD Ib (once), twice a ROD IIa (one case was prior a ROD IIIc), two times a ROD IIIa and three times a ROD IIIb.

Spine Deformity Index (SDI). The SDI of the 26 cases of the control group were within the normal limits as defined by Minne

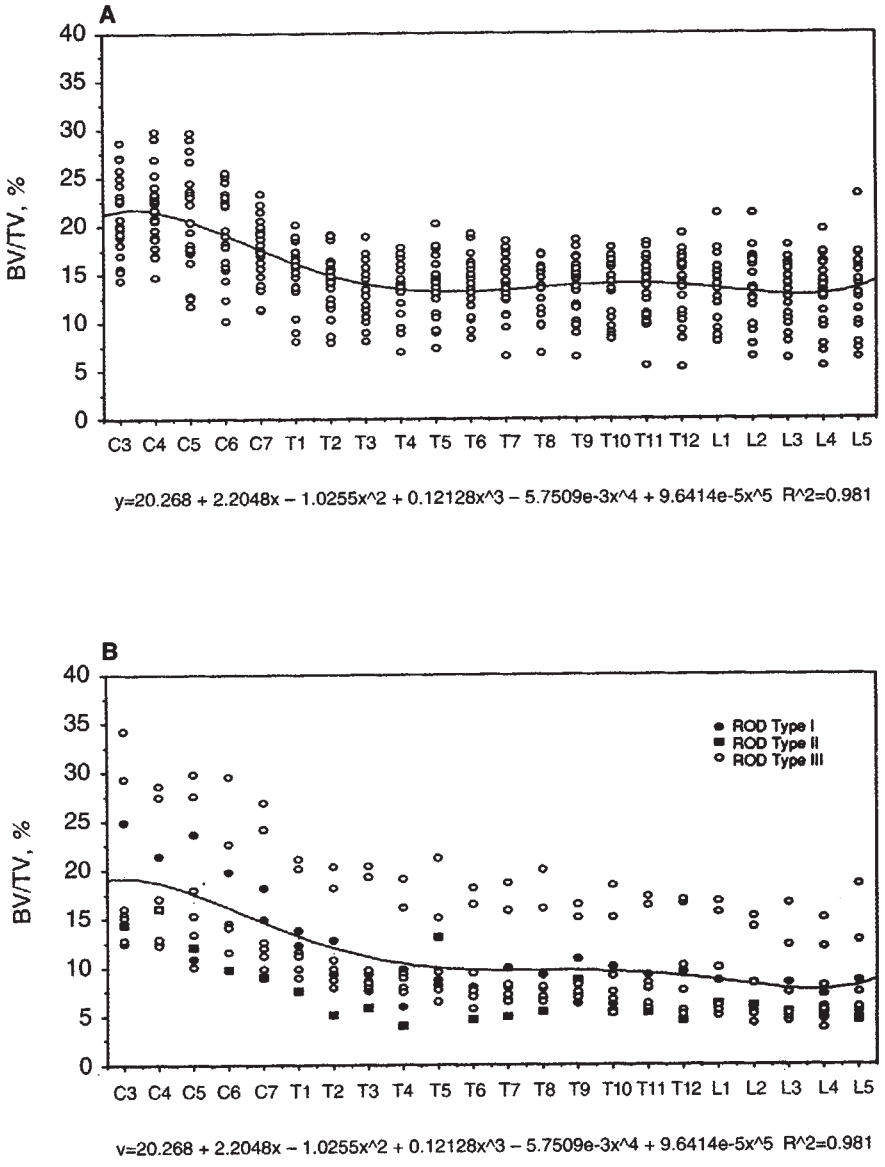


Fig. 3. A. *Distribution of the trabecular bone volume within the spinal columns of 26 skeletally intact patients.* The polynomal through the median values shown as a curve shows a plateau-like course with high BV/TV in the area of cervical spine and clearly lower values for the thoracic and lumbar spine. **B.** Distribution of the trabecular bone volume within the spinal column in cases with renal osteodystrophy. Plateau-like course with highest BV/TV in the cervical spine and reduction in the thoracic and lumbar spine. The mean BV/TV values are equivalent to those of an age-matched control group. Increases in bone volume in the individual curves correspond to vertebral fractures demonstrated in the SDI.

et al [3]. The values of the nine cases with renal osteodystrophy were more widely dispersed. The values which did not fit into the curve indicate deformation of vertebrae. Fractures of vertebrae could be found in particular in ROD types I and II (Fig. 2).

Bone volume (BV/TV). Distribution of the trabecular bone volume (BV/TV) within the spinal column showed a curve, with the highest values in the cervical spine and a decline in the thoracic and lumbar spine. The age-related normal control-group showed a median trabecular bone volume in the cervical spine of 16.7%, in the thoracic spine of 10.3% and in the lumbar spine of 8.8%. In the ROD group, the median values in the cervical spine were 17.5%, in the thoracic spine were 10.2% and in the lumbar spine 8.0% (Fig. 3).

The unsystematic variation of the trabecular bone volume from vertebra to vertebra in the normal control group was 29.4% (16.2 to 43.1%) in the thoracic spine and 17.6% (8.2 to 32.4%) in the lumbar spine. For the cases with renal osteodystrophy the variation of the trabecular bone volume was 38.3% (18.6 to 81.0%) in the thoracic spine and 19.9% (11.3 to 28.3%) in the lumbar spine.

There was a higher trabecular bone volume in the iliac crest in comparison to the lumbar spine. Within the age-related control group the BV/TV was 11.5% in the iliac crest biopsy and 8.8% in the lumbar spine. In the cases with renal osteodystrophy the mean BV/TV in the iliac crest biopsy was 12.0% and in the lumbar spine 8.0%. The correlation of the iliac crest biopsy and the lumbar spine for the trabecular bone volume was $r = 0.83$ ($P < 0.001$) for the normal control group and $r = 0.57$ ($P = 0.11$) for the cases with renal osteodystrophy. An age-related reduction of BV/TV, largely described as linear in bone volume loss syndromes, was not evident for those cases examined with ROD. On the contrary, a

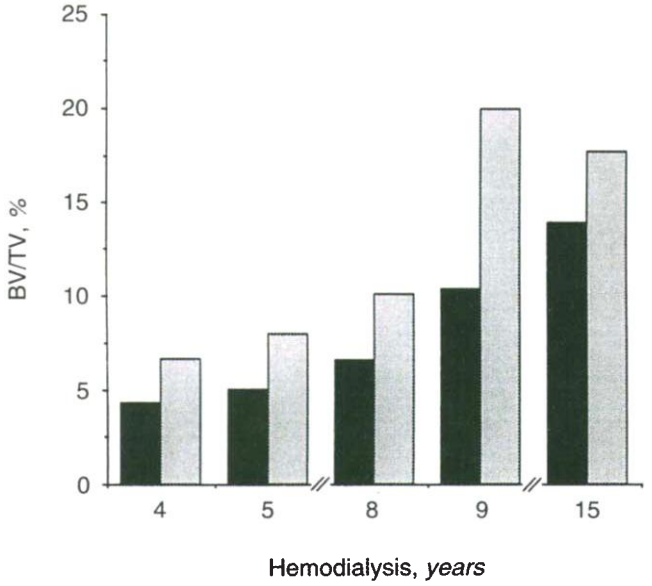


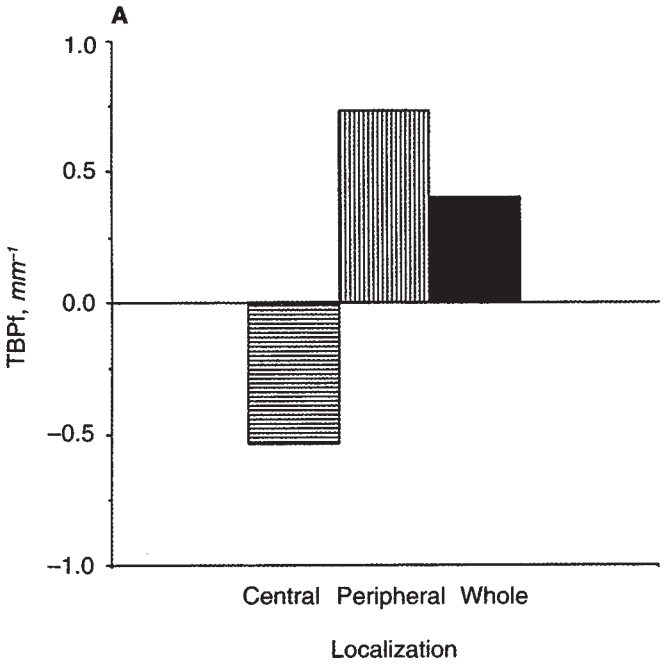
Fig. 4. *Representation of the median trabecular bone volume (BV/TV) of the iliac crest and the lumbar spine in relation to the duration of hemodialysis.* There is an increasing trabecular bone volume with increasing hemodialysis duration. Symbols are: (■) BV/TV lumbar spine; (▨) BV/TV iliac crest biopsy.

longer history of hemodialysis appeared to correspond with higher bone volume (Fig. 4).

Trabecular interconnection, trabecular bone pattern factor (TBPf). Trabecular interconnection, TBPf, varied greatly in the vertebrae depending on the point of measurement. Compared with the central vertebral sections, the intertrabecular linking in the periphery was poorer, in spite of a relatively higher BV/TV. A comparison of BV/TV and TBPf for the second vertebra showed a median TBPf in the periphery of 0.73 mm^{-1} and centrally of -0.54 mm^{-1}, with a median BV/TV of 8.35% in the periphery and 6.78% centrally (Fig. 5). TBPf had a wide range, particularly in renal osteodystrophy and especially in the periphery.

Trabecular thickness (Tb.Th). The trabecular thickness was mostly constant. Neither depended on duration of hemodialysis, type of ROD, nor in correlation to age could significant changes be demonstrated. The median Tb.Th was 120.23 μm in the men examined (control group 126.88 μm) and 134.90 μm in the women (control group 126.72 μm). In all cases, the trabeculae arranged horizontally were thinner than the vertical trabeculae. For types I and II of ROD with a median Tb.Th of 127.9 μm, a thickness of 116.6 μm was shown in the horizontal and 133.5 μm in the vertical trabecular structures. For type III the mean Tb.Th was 126.2 μm, the thickness of the horizontal trabeculae was 116.4 μm and the vertical trabeculae were 131.5 μm. In males this difference averaged to 10.42 μm (9%) and in females to 22.35 μm (17%).

Trabecular number (Tb.N). There was an age-related decrease of the trabecular number from the 30th year of age (0.61 mm^{-1}) to the 80th year of age (0.40 mm^{-1}) of 34.6%. The trabecular number in the age-related control group was 0.48 mm^{-1} ($\pm$ 0.08 mm^{-1}). In ROD the trabecular number varied greatly, ranging between 0.39 mm^{-1} and 1.02 mm^{-1}. The average trabecular number in the cases with renal osteodystrophy was 0.63 mm^{-1} ($\pm$ 0.19 mm^{-1}), which was an increase of 31.3% compared with the age-related control group. With longer histories of



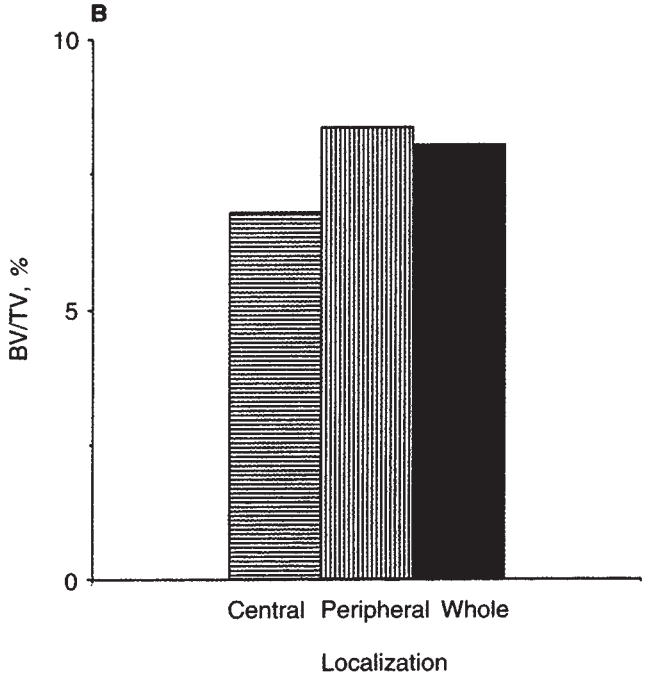
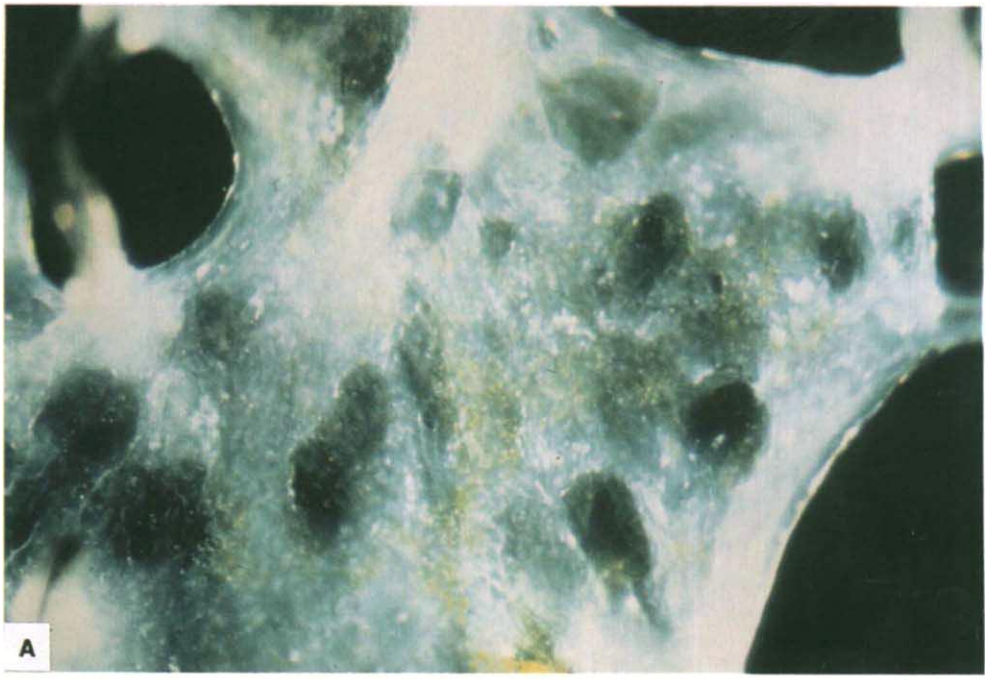


Fig. 5. A. *Image of trabecular interconnection (TBPf) within the spinal column with the example of the 2nd lumbar vertebra.* In renal osteodystrophy, there is clearly better interconnection centrally than in the periphery. **B.** Distribution of trabecular bone volume (BV/TV) in the 2nd lumbar vertebra. With a median central BV/TV of 6.8% there is a peripheral BV/TV of 8.4%. Comparison with TBPf shows that a higher trabecular bone volume does not mean better trabecular interconnection.



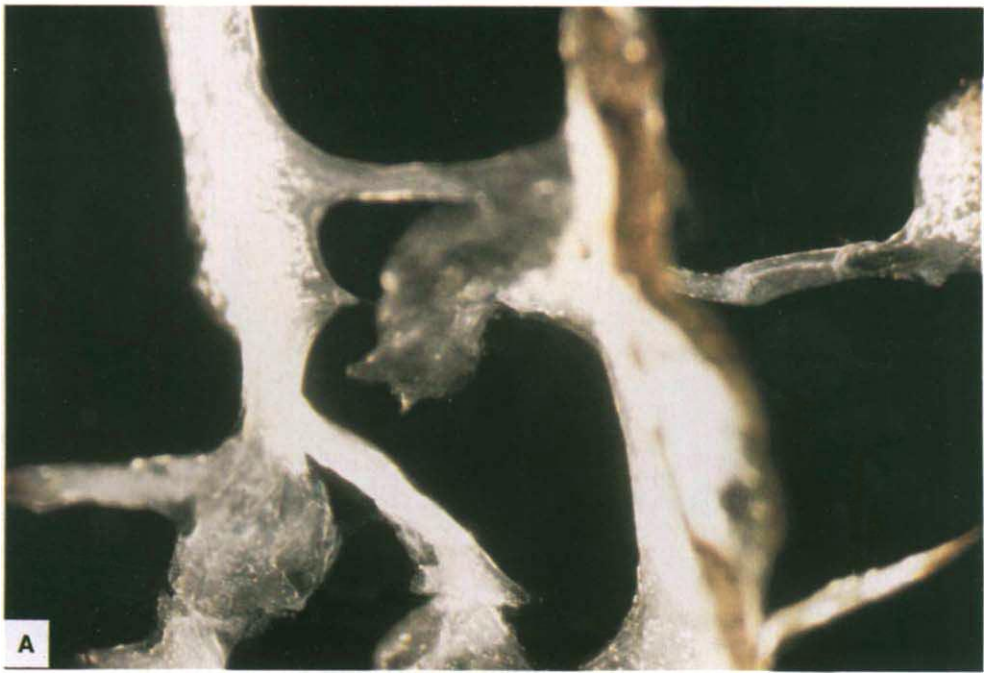


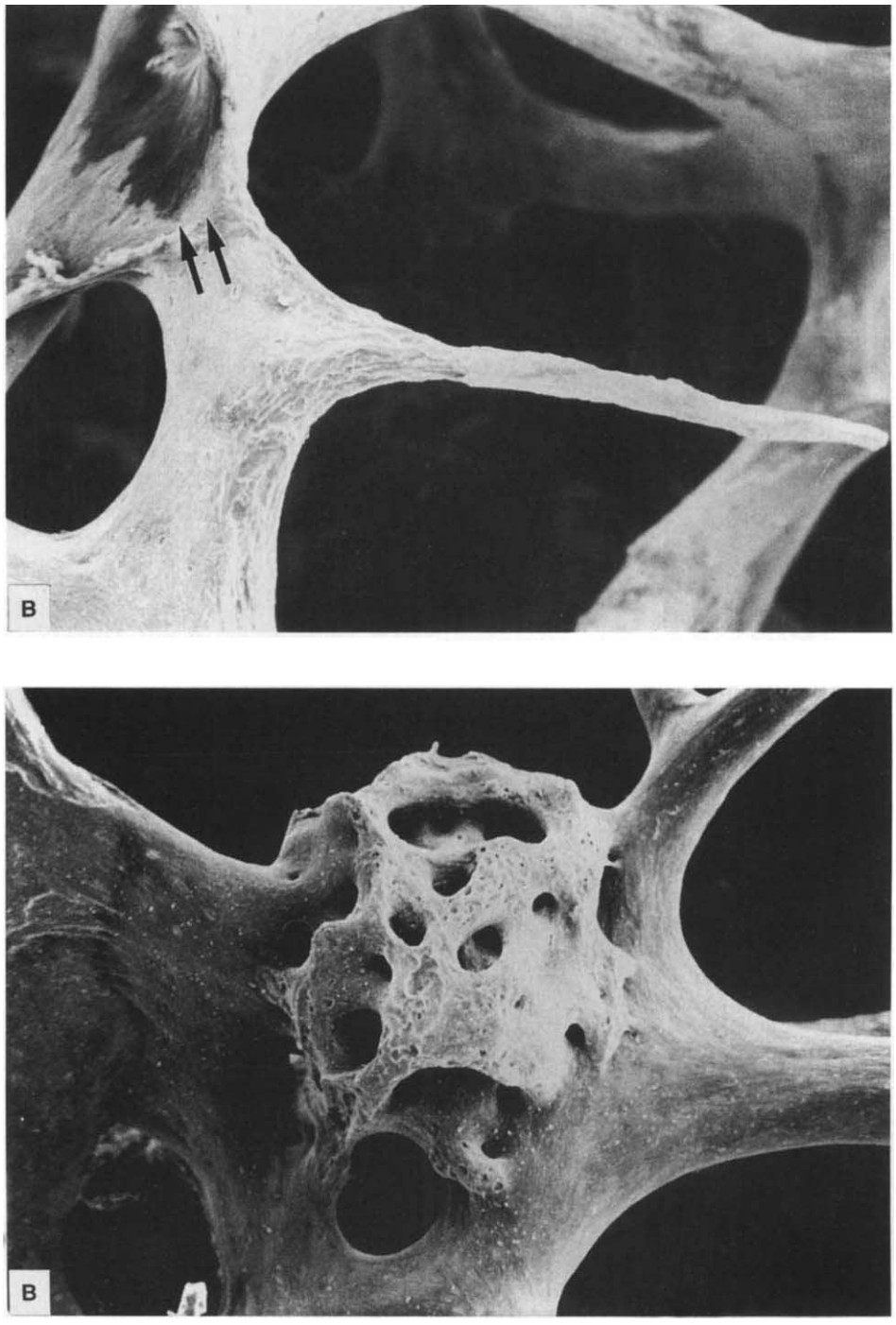
Fig. 6. (Top) *Covered perforations with outline thinning of the mineralized bone.* **A.** Multiple covered perforations by light microscope (magnification 90×). Reproduction of this figure in color was made possible by a grant from Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany. **B. (Facing page, top)** A perforation (arrow) by raster screen microscope (magnification 120×).

Fig. 7. (Bottom) A. *Free plates represent structures with a large mineral content without relevant biomechanical support function (central).* The detail also shows two microcallus formations in the lower left hand portion (magnification 80×). Reproduction of this figure in color was made possible by a grant from Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany. **B. (Facing page, bottom)** Microcallus formation by raster screen microscope (magnification 120×).

hemodialysis higher values were found, while the trabecular number was reduced with increasing age. There was no significant difference depending on sex. There was a mean Tb.N of 0.61 mm^{-1} in males and 0.66 mm^{-1} in females.

Qualitative results

There was a polymorph picture of vertebral spongiosa in renal osteodystrophy. In the majority of cases examined, there tended to be an accumulation of rod-like structures in the periphery,



Figs. 6, 7. *Continued.*

where central plates were the predominant structural element. The size of the plates could measure up to several square millimeters.

Perforations could be found in all cases, in plates and rods. Particularly the central plates showed a large number of perforations, in various extents and stages. Outlined bone thinning appeared as covered perforations (Fig. 6). Tunneling resorption could be seen on the stained surface in rods and plates. As a result of the various perforations, free ends were found as an expression of reduced trabecular stability. Apart from rod-like free ends, free ending plates were quite unusual (Fig. 7). Microcallus formations could regularly be found in the peripheral vertebral sections. They were most often seen in rods, or in rod nodes. More seldomly, they were seen in the area of plate intersections. On the whole, an

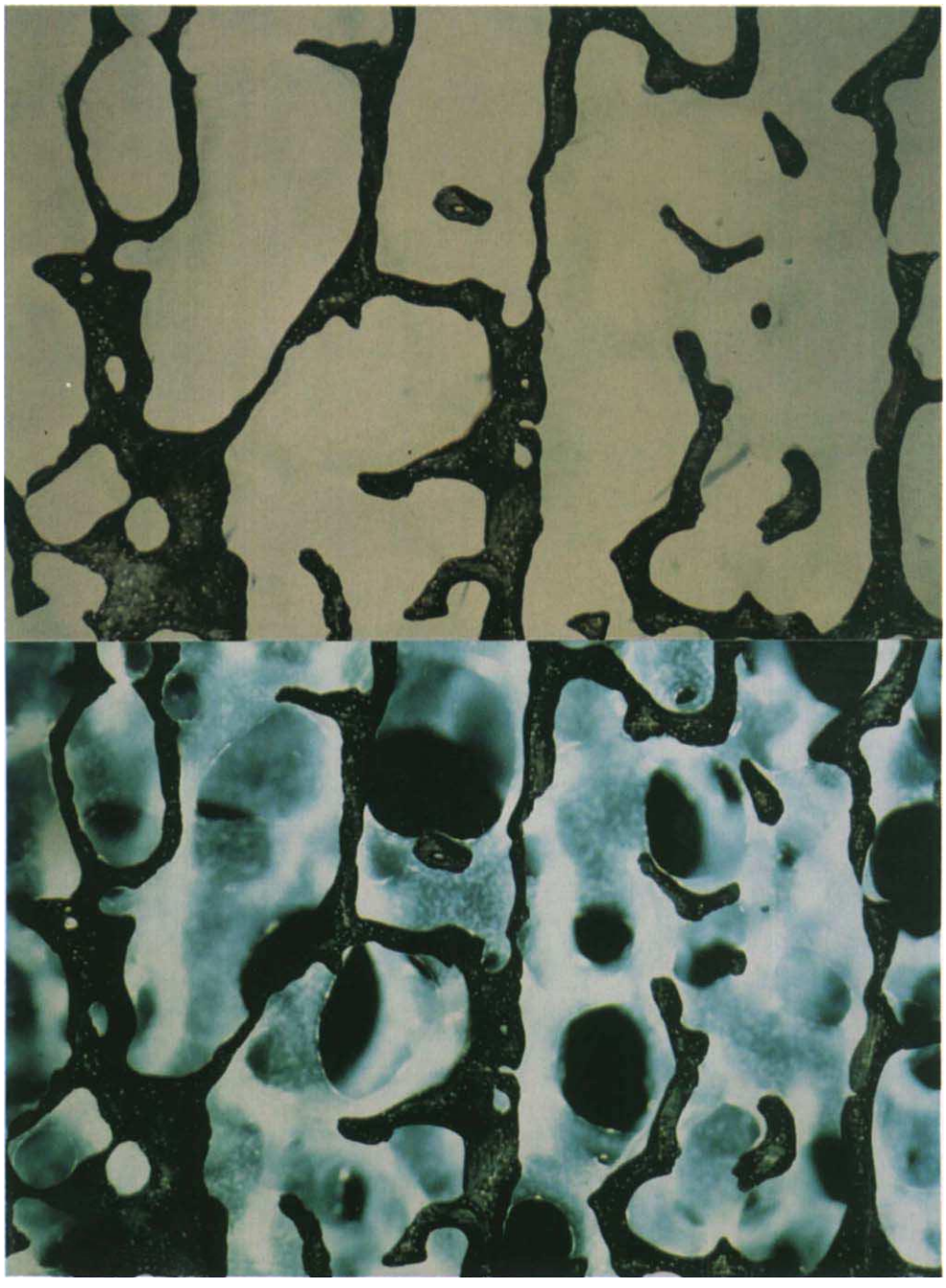


Fig. 8. *Surface stained block grinding from the vertebra of a skeletally intact patient of the control group.* Two-dimensional image of the spongiosa structure. In the dark field the continuation of the structures which were cut into is visible (magnification 20×). Reproduction of this figure in color was made possible by a grant from Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany.

irregular spongiosa was seen with at times bizarre trabecular structures, of which there is not yet any exact analysis or definition (Figs. 8 and 9).

Discussion

Experimental presentations of the trabecular structure are often based on histomorphological examination of the iliac crest biopsy slide material. The value of these studies is very limited [8]. This is due to the completely different biomechanical conditions in the pelvis and the spinal column, and due to the fact that it is impossible to correlate the trabecular pattern of a section with the actual configuration of the structure. Thus a combined two- and three-dimensional analysis of the whole spinal column from C2 to L5 was carried out [6, 9]. The extraordinarily complex spongiosa structures in ROD are particularly evident in the three-dimensional evaluation.

In the pathogenesis of ROD, a deciding factor is the parathyroid hormone as well as parathyroid hormone resistance and

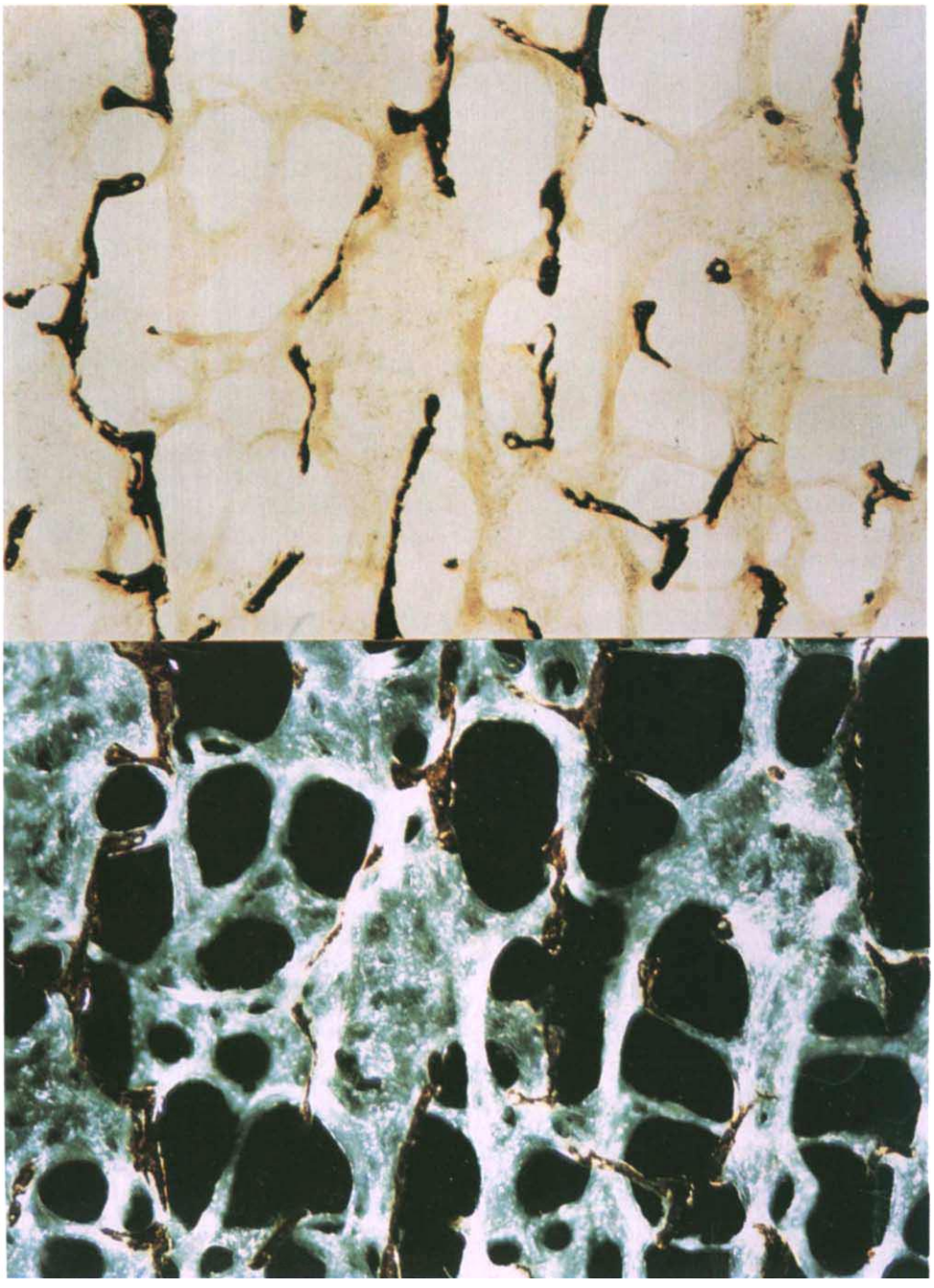


Fig. 9. *Irregular spongiosa in the light field and dark field.* The bizarre trabecular structures are the expression of disturbed remodeling in ROD (ROD Type IIIb) (magnification 10×). Reproduction of this figure in color was made possible by a grant from Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany.

vitamin D deficiency [5]. Parfitt [10] has previously described as early as 1976 in studies on animals that the parathyroid hormone, depending on dose and length of administration, can cause osteopenia and osteosclerosis. The contradictory statements on BV/TV with primary hyperparathyroidism (pHPT) [11, 12] appear to confirm this. Vogel showed in 1988 [13] an increase in BV/TV of 34 to 42% in 92 iliac crest biopsies and explained this with a 25 to 30% greater trabecular width and a decreased frequency of perforations due to pHPT.

An increase of BV/TV for ROD, in comparison to the control group, cannot generally be confirmed. The distribution within the spinal column is comparable to that of the control group. Nevertheless, the longer the hemodialysis, the greater the apparent increase in trabecular bone volume. A decrease in BV/TV corresponding to age, as has been described for the skeletally intact [9, 14, 15], is not evident. The main architectural elements are plates in the center and rods (sticks) in the periphery. However, in general it is not possible to predict different bone volume for

certain vertebral areas. Consequently, in contrast to studies in normal groups [9], in ROD stick-like structures influence the BV/TV.

In 1985 Kleerekoper et al [16] found similar bone volume in patients with osteoporosis and in the skeletally intact and thus concluded from this, that BV/TV cannot be the only determining factor for distinguishing between physiological and pathological skeletal status.

Mautalen et al [17] confirmed these results in 1990. In 1987, Compston et al [18] theorized that the degree of intertrabecular linking was decisive. In 1991 Hahn et al [4] described a parameter for the simple quantification of the networking using TBPf.

Renal osteodystrophy presents with a pathologically-diminished trabecular interconnection though trabecular bone volume is within normal limits. Due to the formation of irregular spongiosa, the validity of TBPf in ROD is limited. The results are influenced by concave and convex structures which exceed the bounds of intertrabecular nodes, plates, rods and perforations.

SDI demonstrates vertebral fractures in ROD types I and II. According to the results available, there is no increased risk of vertebral fractures for type III. Wilson et al [19] also show no increased fracture risk in a statistical evaluation of x-rays in pHPT. Osseous peculiarities of chronic renal failure are changes in the micro-architecture as a result of the disturbed function of bone cells. The fractures which occur in ROD type I and II cannot be explained solely by the trabecular bone volume, but indicate a diminished load-bearing capacity of the spongiosa in ROD.

Perforations, as well as progressive thinning, were described by Parfitt et al [20] in 1983 as the origin of trabecular loss. Classic perforations, tunnel perforations and hidden perforations occur. There is a hypothesis to explain the origin of perforations due to "killer osteoclasts" [7]. These osteoclasts make a deeper "footprint" in the trabecular, which measures 100 to 150 μm instead of the usual 60 μm. How osteocytes are related to perforations and whether plates are just material storers is not yet known, nor whether one must distinguish between physiological and pathological perforations.

The trabecular thickness is mostly constant in those patients with renal osteodystrophy. With a thickness of 120.23 μm in males and 134.90 μm in females there is no significant difference to the control group (males 126.88 μm, females 126.72 μm). Changes cannot be shown to be related to age, length of hemodialysis or type of ROD. The difference in the trabecular thickness depends on the direction of the trabeculae (horiz/vert). Thus vertically running spongiosa structures, with an absolute median difference of 10.42 μm in males and 22.35 μm in females, are broader than those running horizontally. But the trabecular number varies greatly: with a mean Tb.N value of 0.63 mm^{-1}, the range lies between 0.39 mm^{-1} and 1.02 mm^{-1}. These differences cannot be explained by remodeling. The only explanation may be modeling processes with strong resorption and a high degree of new bone formation through microcallus and bridging-callus. The role of a parathyroid hormone resistance, developing in the course of the disease, for the microarchitectural changes is currently unknown.

Plates and rods are the predominant structures in trabecular bone. The rods are formed mainly through perforating, restructuring processes in plates, as Parfitt et al [20] already suspected in 1983. This hypothesis can be confirmed through the documentation of the various forms and stages of perforation in renal osteodystrophy. Evidence of free plates is certainly a peculiarity. Free rods, microcallus and bizarre trabeculae are structures with no functional stability in spite of their same radiological density. In the periphery, the second principle of rod formation is visible, which is the *de novo* synthesis by bridging-callus.

Microcallus formations in osteoporosis at an advanced age are described by Aaron et al [21]. This is a local bone reorganization with far greater dynamism than is possible with normal basic metabolic units (BMU's). Microcallus is observed particularly at the intersection of two rods, but also at the point where rods and plates cross. In ROD there is an accumulation of microcallus formations in the periphery, near the endplates. This is modeling in an extreme form. The picture is characterized by micro- and bridging-callus and also consecutive newly formed trabeculae. From the pathomorphological aspect, this correlates with the sclerosis, radiographically described by Chan et al [22] and Young et al [23] in vertebrae of patients with renal osteodystrophy.

In all cases, in the region of the iliac crest biopsy a higher BV/TV is found than in the corresponding lumbar spine. The correlation of the trabecular bone volume of the iliac crest to the lumbar spine in ROD is $r = 0.57$. This is of particular clinical relevance, as biopsy studies from the region of the os ilium can only provide information on the status of the decisive osseous organ, the spine, when there is an understanding of the relation between iliac crest and spinal column.

The three-dimensional changes in the spongious microarchitecture are far more marked in ROD than was until now suspected from histological slide material. At present it must be assumed that structural loss and structural changes are irreversible. Therapeutic concepts must, from a morphological point of view, always be directed towards prevention since the reconstruction of a "normal" three-dimensional structure by regular remodeling is not currently possible.

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References

1. Bordier P, Matrajt H, Miravet L, Hioco D: Measure histologique de la mass et de la resorption des travees osseouses. *Path Biol* 12:1238–1243, 1964
2. Hahn M, Vogel M, Delling G: Undecalcified preparation of bone tissue: Report of technical experience and development of new methods. *Virchows Arch A Pathol Anat* 418:1–7, 1991
3. Minne HW, Leidig G, Wüster C, Siromachkostov L, Baldauf G, Bickel R, Sauer P, Lojen M, Ziegler R: A newly developed spine deformity index (SDI) to quantitate vertebral crush fractures in patients with osteoporosis. *Bone Miner* 3:335–350, 1988
4. Hahn M, Vogel M, Delling G: Trabecular bone pattern factor—A new parameter for simple quantification of bone microarchitecture. *Bone* 13:327–330, 1992
5. Delling G: *Endokrine Osteopathien.* Fischer, Stuttgart, 1975
6. Delling G, Vogel M, Wieland U, Pompesius-Kempa M, Hahn M: Trabecular bone structure in human spine—Results of a new 2- and

3-dimensional analysis, in *Bone Morphometry*, Niigata, Nishimura Smith-Gordan, 1988, pp 256–259, 1990
7. DELLING G, VOGEL M, HAHN M: Morphologische Mechanismen für die Regulation der Knochenstruktur. *Nieren- und Hochdruckkrankheiten* 6:255–261, 1991
8. WRIGHT CDP, CRAWLEY EO, EVANS WD, GARRAHAN NJ, MELLISH RWE, CROUCHER PI, COMPSTON JE: The relationship between spinal trabecular bone mineral content and iliac crest trabecular volume. *Calcif Tissue Int* 46:162–165, 1990
9. VOGEL M, HAHN M, POMPESIUS-KEMPA M, DELLING G: Trabecular microarchitecture of the human spine. *Neuere Ergebnisse in der Osteologie,* edited by WILLERT H, HEUCK FHW, Heidelberg, Springer Verlag, 1989, pp 449–455
10. PARFITT AM: The actions of parathyroid hormone on bone: Relation to bone remodelling and turnover, calcium homeostasis, and metabolic bone disease. *Metabolism* 25:1033–1069, 1976
11. ERIKSEN EF, MOSEKILDE L, MELSEN F: Trabecular remodeling and balance in primary hyperparathyroidism. *Bone* 7:213–219, 1986
12. TAM CS, BAYLEY A, CROSS EG: Bone apposition in primary hyperparathyroidism measurements based on short interval tetracycline labeling of bone. *Metabolism* 31:759–762, 1982
13. VOGEL M: Neuere Ergebnisse über den regulativen Einfluß von Parathormon auf die Spongiosastruktur beim primären Hyperparathyreoidismus. *Endokrinologie* 12:67–68, 1988
14. MALLUCHE H, SHERMAN D, MEYER W, MASSRY SG: Quantitative bone histology in 84 normal American subjects. *Calcif Tissue Int* 34:449–455, 1982
15. MOSEKILDE L: Age-related changes in vertebral trabecular bone architecture—assessed by a new method. *Bone* 9:247–250, 1988
16. KLEEREKOPER M, VILLANUEVA AR, STANCIU J, RAO SD, PARFITT AM: The role of three-dimensional trabecular microstructure in the pathogenesis of vertebral compression fracture. *Calcif Tissue Int* 37:594–597, 1985
17. MAUTALEN C, VEGA E, GHIRINGHELLI G, FROMM G: Bone diminution of osteoporotic at different skeletal sites. *Calcif Tissue Int* 46:217–221, 1990
18. COMPSTON JE, MELLISH RWE, GARRAHAN NJ: Age-related change in iliac crest trabecular microanatomic bone structure in man. *Bone* 8:289–292, 1987
19. WILSON RJ, RAO S, ELLIS B, KLEEREKOPER M, PARFITT AM: Mild asymptomatic primary hyperparathyroidism is not a risk factor for vertebral fractures. *Ann Intern Med* 109:959–962, 1988
20. PARFITT AM, MATHEWS CHE, VILLANUEVA AR, KLEEREKOPER M, FRAME B, RAO DS: Relationship between surface, volume and thickness of iliac trabecular bone in aging and osteoporosis. *J Clin Invest* 72:1396–1409, 1983
21. AARON JE, MAKINS NB, FRANCIS RM, PEACOCK M: Microanatomic and histological changes associated with trabecular bone loss with ageing and osteoporosis. *Clin Orthop Rel Res* 213:260–271, 1987
22. CHAN YL, FURLONG TJ, CORNISH CJ, POSEN S: Dialysis osteodystrophy. A study involving 94 patients. *Medicine* 64:296–309, 1985
23. YOUNG W, SEVCIK M, TALLROTH K: Metaphyseal sclerosis in patients with chronic renal failure. *Skeletal Radiol* 20:197–200, 1991